pable of binding to a region in the SRCR domains I-II of the CD163 receptor, or a variant thereof

It is preferred that the Hp-Hb complex or a part thereof or a mimic thereof is available in a purified and/or isolated form.

According to the invention the term "Hp-Hb complex" is meant to include functional equivalents of the Hp-Hb complex comprising a predetermined amino acid sequence. In the present context the term "predetermined amino acid sequence of Hp-Hb complex" relates to both the haptoglobin sequence and the haemoglobin sequence.

The predetermined sequence of a haptoglobin chain may be any of the sequences shown in Fig. 4a and 4b, i.e. any of the sequences having the sequence identification in the sequence database SWISS-PROT (sp) or trEMBL (tr).

15

10

sp|P00737|HPT1_HUMAN sp|P00738|HPT2_HUMAN sp|P60417|HPT_ATEGE tr|Q60574|Q60574 tr|Q61646|Q61646 sp|Q62558|HPT_MUSSA sp|P06886|HPT_RAT tr|O35086|O35086

spIP19006IHPT CANFA

25

35

20

A predetermined amino acid sequence for a heamoglobin chain may be any of the sequences mentioned below together with accession No. in the sequence database SWIS-SPROT:

30 sp|P01922|HBA_HUMAN HEMOGLOBIN ALPHA CHAIN – Homo sapiens (Human), Pan troglodytes (Chimpanzee), and Pan paniscus (Pygmy chimpanzee) (Bonobo).

VLSPADKTNVKAAWGKVGAHAGEYGAEALERMFLSFPTTKTYFPHFDLSH GSAQVKGHGKKVADALTNAVAHVDDMPNALSALSDLHAHKLRVDPVNFKL LSHCLLVTLAAHLPAEFTPAVHASLDKFLASVSTVLTSKYR

sp|P02023|HBB_HUMAN HEMOGLOBIN BETA CHAIN -

Homo sapiens (Human), Pan troglodytes (Chimpanzee), and Pan paniscus (Pygmy chimpanzee) (Bonobo).

VHLTPEEKSAVTALWGKVNVDEVGGEALGRLLVVYPWTQRFFESFGDLST

5 PDAVMGNPKVKAHGKKVLGAFSDGLAHLDNLKGTFATLSELHCDKLHVDP
ENFRLLGNVLVCVLAHHFGKEFTPPVQAAYQKVVAGVANALAHKYH

sp|P02042|HBD_HUMAN HEMOGLOBIN DELTA CHAIN – Homo sapiens (Human).

10

VHLTPEEKTAVNALWGKVNVDAVGGEALGRLLVVYPWTQRFFESFGDLSS
PDAVMGNPKVKAHGKKVLGAFSDGLAHLDNLKGTFSQLSELHCDKLHVDP
FNFRI I GNVLVCVLARNFGKEFTPQMGAAYQKVVAGVANALAHKYH

15

splP02096|HBG_HUMAN HEMOGLOBIN GAMMA-A AND GAMMA-G CHAINS - Homo sapiens (Human), and Pan troglodytes (Chimpanzee).

20

GHFTEEDKATITSLWGKVNVEDAGGETLGRLLVVYPWTQRFFDSFGNLSS
ASAIMGNPKVKAHGKKVLTSLGDAIKHLDDLKGTFAQLSELHCDKLHVDP
ENFKLLGNVLVTVLAIHFGKEFTPEVQASWQKMVTAVASALSSRYH

sp|P09105|HBAT_HUMAN HEMOGLOBIN THETA-1 CHAIN – Homo sapiens (Human).

25

ALSAEDRALVRALWKKLGSNVGVYTTEALERTFLAFPATKTYFSHLDLSP GSSQVRAHGQKVADALSLAVERLDDLPHALSALSHLHACQLRVDPASFQL LGHCLLVTLARHYPGDFSPALQASLDKFLSHVISALVSEYR

30

sp|P02008|HBAZ_HUMAN HEMOGLOBIN ZETA CHAIN – Homo sapiens (Human).

SLTKTERTIIVSMWAKISTQADTIGTETLERLFLSHPQTKTYFPHFDLHP GSAQLRAHGSKVVAAVGDAVKSIDDIGGALSKLSELHAYILRVDPVNFKL LSHCLLVTI AARFPADFTAFAHAAWDKFLSVVSSVLTEKYR

35

sp|P02100|HBE_HUMAN HEMOGLOBIN EPSILON CHAIN – Homo sapiens (Human).

VHFTAEEKAAVTSLWSKMNVEEAGGEALGRLLVVYPWTQRFFDSFGNLSS
PSAILGNPKVKAHGKKVLTSFGDAIKNMDNLKPAFAKLSELHCDKLHVDP
ENFKLI GNVMVIII ATHEGKFFTPEVQAAWOKLVSAVAIALAHKYH

tr|Q14510|Q14510 SICKLE BETA-HEMOGLOBIN MRNA – Homo sapiens (Human).

MVHLTPVEKSAVTAXWGKVNVDEVGGEALGRLLVVYPWTQRFFESFGDLS
TPDAVMGNPKVKAHGKKVLGAFSDGLAHLDNLKGTFATLSELHCDKLHVD
PENERI I GNVI VCVLAHHEGKEFTPPVQAAYQKVVAGVANALAHKYH

A "functional equivalent" is defined as:

- equivalents comprising an amino acid sequence capable of being recognised by an antibody also capable of recognising the predetermined amino acid sequence, and/or
- equivalents comprising an amino acid sequence capable of binding to a receptor moiety also capable of binding the predetermined amino acid sequence, and/or
- equivalents having at least a substantially similar or higher binding affinity to CD163 as at least a monomeric Hp-Hb complex comprising said predetermined amino acid sequence.

According to the present invention a functional equivalent of a Hp-Hb complex or fragments thereof may be obtained by addition, substitution or deletion of at least one amino acid in either or both of the haptoglobin sequence and the haemoglobin sequence. Thus, a functional equivalent of the Hp-Hb complex may comprise a modification of either of the components of the complex or both.

When the amino acid sequence comprises a substitution of one amino acid for another, such a substitution may be a conservative amino acid substitution. Fragments of the complex according to the present invention may comprise more than one such substitution, such as e.g. two conservative amino acid substitutions, for example three or four conservative amino acid substitutions, such as five or six conservative amino acid substitutions, for example seven or eight conservative amino acid substitutions, for example from 15 to 25 conservative amino acid substitutions. Substitutions can be made within any one or more groups of predetermined amino acids.

25

30

35

20

5

10

15